Please amend the application as follows:

In the Specification

Please replace the paragraph at page 6, lines 15-26 with the following paragraph.

As described in the examples, a gene which encodes a cell membrane-associated ligand which is present in the nervous system and the vascular system has been shown, in adult mice, to be expressed by arterial endothelial cells, and not by venous endothelial cells. Further, the gene which encodes the receptor for the ligand has been shown to be expressed by venous endothelial cells, but not by artery cells. Thus, for the first time, a marker found on arterial endothelial cells (an artery-specific marker) and a venous endothelial cell- (vein-specific) marker are available, making it possible to distinguish between arteries and veins for a variety of purposes, such as further study and understanding of the mechanisms of blood vessel formation; selective targeting of treatments or therapies to arteries or veins (targeting to arteries but not veins or vice versa) and selective modulation (enhancement or inhibition) of formation, growth and survival of arteries and/or veins.

a1

Please replace the paragraph at page 10, lines 3-7 with the following paragraph.

As used herein, a transgenic mouse is one which has, incorporated into the genome of some or all of its nucleated cells, a genetic alteration which has been introduced into the mouse or at least one of its ancestors, by the manipulations of man. A transgenic mouse can result, for example, from the introduction of DNA into a fertilized mouse ovum or from the introduction of DNA into embryonic stem cells.

a2

Please replace the paragraph at page 13, line 18 through page 14, line 9 with the following paragraph.

As a result of the work described herein, it is possible to differentiate between arterial endothelial cells (arteries) and venous endothelial cells (veins) by taking advantage of the

a3

presence of an artery-specific or vein-specific gene product on the surface of the cells. Arterial endothelial cells and venous endothelial cells can each be isolated from cells of other tissue types by, for instance, excision of artery or vein tissue from a sample of mammalian tissue, dissociation of the cells, allowing the cells to bind, under appropriate conditions, to a substance which has some property or characteristic (e.g., a molecule which provides a label or tag, or molecule that has affinity for both an artery-specific cell surface protein and another type of molecule) that facilitates separation of cells bound to the substance from cells not bound to the substance. Separation of the cells can take advantage of the properties of the bound substance. For example, the substance can be an antibody (antiserum, polyclonal or monoclonal) which has been raised against the protein specific to arterial endothelial cells (or to a sufficiently antigenic portion of the protein) and labeled with a fluorochrome, with biotin, or with another label. Separation of cells bound to the substance can be by fluorescence activated cell sorting (FACS), for a fluorescent label, by streptavidin affinity column, for a biotin label, by other affinity-based separation methods, or, for example, by antibody-conjugated magnetic beads or solid supports. "Isolated" as used herein for cells indicates that the cells have been separated from other cell types so as to be a population enriched for a certain cell type, compared to the starting population, and is not limited to the case of a population containing 100% one cell type.

a3 cont

Please replace the paragraph at page 17, line 26 through page 18, line 12 with the following paragraph.

A drug that inhibits interaction of an artery-specific cell surface molecule (e.g., an arterial endothelial cell-specific surface molecule) with a vein-specific cell surface molecule (e.g., a venous endothelial cell-specific surface molecule) can be identified by a method in which, for example, the arterial endothelial cell-specific surface molecule and the venous endothelial cell-specific surface molecule are combined with a drug to be assessed for its ability to inhibit interaction between the cell-specific molecules, under conditions appropriate for interaction between the cell-specific molecules. The cell-specific molecules may be used in the assay such that both are found on intact cells in suspension (e.g., isolated arterial or venous endothelial cells, immortalized cells derived from these, or cells which have been modified to express an artery- or vein-specific cell surface molecule); one cell type is fixed to a solid support, and the other

a4

molecule, specific to the other cell type, is in soluble form in a suitable solution; or the molecule specific to one cell type is fixed to a solid support while the molecule specific to the other cell type is found free in a solution that allows for interaction of the cell-specific molecules. Other variations are possible to allow for the convenient assessment of the interaction between the two different cell-specific molecules.

a4 cont

Please replace the paragraph at page 23, lines 7-23 with the following paragraph.

The differential expression of EphrinB2 in arteries and of EphB4 in veins allows for the specific targeting of drugs, diagnostic agents, imaging agents, or other substances to the cells of arteries or of veins. A targeting vehicle can be used for the delivery of such a substance. Targeting vehicles which bind specifically to EphrinB2 or to EphB4 can be linked to a substance to be delivered to the cells of arteries or veins, respectively. The linkage can be via one or more covalent bonds, or by high affinity non-covalent bonds. A targeting vehicle can be an antibody, for instance, or other compound which binds either to EphrinB2 or to EphB4 with high specificity. Another example is an aqueously soluble polypeptide having the amino acid sequence of the extracellular domain of EphB4, or a sufficient portion of the extracellular domain (or a polypeptide having an amino acid sequence conferring a similar enough conformation to allow specific binding to EphrinB2), which can be used as a targeting vehicle for delivery of substances to EphrinB2 in arteries. Similarly, a soluble polypeptide having the amino acid sequence of the extracellular domain of EphrinB2 or a sufficient antigenic portion of the extracellular domain (or a polypeptide having an amino acid sequence conferring a similar enough conformation to allow specific binding to EphB4), can be used to target substances to EphB4 in veins.

a5

Please replace the paragraph at page 32, lines 6-11 with the following paragraph.

Defects in yolk sac angiogenesis were apparent by E9.0 and obvious at E9.5. There was an apparent block to remodeling at the capillary plexus stage, for both arterial vessels, as revealed by β-galactosidase staining, and venous vessels in the anterior region of the sac, as revealed by PECAM staining. Thus, disruption of the *EphrinB2* ligand gene caused both a non-

a6